UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,225	10/05/2007	Jenny Berglund	2676-7992US	3408

24247 7590 02/27/2009

TRASK BRITT
P.O. BOX 2550
SALT LAKE CITY, UT 84110

EXAMINER	
GOON, SCARLETT Y	
ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
02/27/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTOMail@traskbritt.com

Office Action Summary	Application No.	Applicant(s)	
	10/594,225	BERGLUND ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2008*.

2a)☐ This action is FINAL. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-36* is/are pending in the application.

4a) Of the above claim(s) *15-18,24-27 and 33-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-14,19-23 and 28-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *16 December 2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicants' Amendment and Remarks filed on 16 December 2008 in which claims 1-9 were cancelled, and new claims 19-36 are added.

The declaration of Dr. Julie Bouckaert (inventor), submitted by Applicants on 16 December 2008 under 37 CFR § 1.132, is acknowledged and will be further discussed below.

Claims 9-36 are pending in the instant application.

Priority

This application is a National Stage entry of PCT/EP2005/051364 filed on 23 March 2005 and claims priority to EPO foreign application 04101199.0 filed on 23 March 2004. A certified copy of the foreign priority document in English has been received.

Information Disclosure Statement

The information disclosure statement (IDS) dated 16 December 2008 complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Accordingly, it has been placed in the application file and the information therein has been considered as to the merits.

Election/Restrictions

Newly added claims 19-23 and 28-32 read on the previously elected species and will be examined with previously presented claims 10-14 herein.

Claims 15-18 were previously withdrawn from further consideration in the Office Action dated 18 August 2008 pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Claims 24-27 and 33-36 are presently withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Claims 10-14, 19-23 and 28-32 are examined on its merits herein.

The following are new ground(s) of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-14, 19-23 and 28-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over journal publication by Nagahori *et al.* (of record) in view of book publication by Silverman (PTO-892, Ref. U).

Nagahori *et al.* teach the inhibition of adhesion of type 1 fimbriated *Escherichia coli* to various mono-, di- and trivalent mannosides. Many bacteria, including pathogenic ones, express carbohydrate-specific adhesion on their fimbriae. These fimbrial adhesins are often implicated in the initial recognition/binding of bacteria to host cells or persisting colonization of bacteria on certain host cell surfaces. The mannose-specific adhesion of type 1 fimbriated *E. coli* (known as the FimH protein) is known to cause common urinary tract infection (p. 836, column 1, paragraph 1). High-affinity ligands for these adhesins may be useful as therapeutics for preventing or mitigating pathological symptoms (p. 836, column 1, paragraph 2). Compounds that were tested for inhibition towards binding of ^{125}I-Man_{21}-ALK-HSA to *E. coli* include methyl-mannopyranoside, ethyl-mannopyranoside, p-nitrophenyl-mannopyranoside, as well as trivalent mannose compounds, divalent mannose compounds, neoglycoproteins, and dendrimers (p. 839, Table 3 and Table 4; p. 840 Table 5). The results of their study indicated that the presence of the α-mannose configuration enhances the affinity of the compound tremendously (p. 840, subheading "Discussion", paragraph 1). It appears that the β-oriented aglycon does not make good contact with the hydrophobic surface (p. 841, column 1, first full paragraph). The results also indicate that either a long aliphatic chain or an aromatic ring immediately next to the mannose sugar produces the best inhibitors (p. 836, paragraph 2). Nagahori *et al.* conclude that in designing a potential inhibitor of *E. coli* adhesion that is medically applicable, it is obviously prudent to incorporate a long aliphatic chain or an aromatic residue immediately next to

mannose (p. 841, column 2, second full paragraph). The affinity can also be further enhanced by multivalency, such as by using dendrimers or neoglycoproteins.

With respect to the limitation of instant claims 11, 20 and 29, the terms pilus and fimbriae are commonly used interchangeably (Salyers *et al.*, of record).

Nagahori *et al.* do not explicitly teach the mannopyranoside species, heptyl-α-D-mannopyranoside, elected by the applicants. However, as discussed above, Nagahori *et al.* do explicitly indicate that a potential inhibitor of *E. coli* adhesion that is medically applicable would incorporate a long aliphatic chain or an aromatic residue immediately next to mannose (p. 841, column 2, second full paragraph). Furthermore, Silverman teach that the biological properties of homologous compounds show regularities of increase and decrease. For many series of compounds, lengthening of a saturated carbon side chain from one (methyl) to five to nine carbon atoms (pentyl to nonyl) produces an increase in pharmacological effects, while further lengthening results in a sudden decrease in potency (p. 16, subheading "Homologation").

As such, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Nagahori *et al.*, concerning medically applicable inhibitors of *E.coli* adhesion that incorporates an α-linked long aliphatic chain or an aromatic group at the anomeric position of mannose, with the teachings of Silverman, regarding the biological properties of homologous compounds. Since Nagahori *et al.* teach that α-linked long aliphatic chains on the anomeric position of mannose would be applicable inhibitors of *E. coli* adhesion, one would have been motivated to combine the teachings of Nagahori *et al.* with Silverman in order to receive

the expected benefit, as suggested by Silverman, that lengthening of a saturated carbon side chain from one carbon atom to five to nine carbon atoms, produces an increase in pharmacological effects.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Response to Arguments

Applicant's arguments filed 16 December 2008 and the declaration of Dr. Julie Bouckaert, submitted on 16 December 2008 under 37 CFR § 1.132, with respect to the rejection of claims 10-14 made under 35 USC § 103(a) as being unpatentable over Nagahori *et al.*, in view of Choudhury *et al.*, in view of Bouckaert, have been fully considered but are moot in view of the new ground of rejection above.

Specifically, Applicants argue that although Nagahori *et al.* suggest the use of a long aliphatic chain or an aromatic ring immediately next to the mannose sugar to produce the best inhibitors, Nagahori *et al.* do not indicate how long a "long" aliphatic chain should be. This argument is moot in view of the applied secondary reference by Silverman above. As indicated in the rejection above, Silverman teach that lengthening of a saturated carbon side chain from one carbon to five to nine carbon atoms produces an increase in pharmacological effects. Thus, the claimed invention as a whole is *prima facie* obvious over the teachings of the prior art.

Applicants further argue that holding n-pentyl obvious would amount to an "obvious to try" standard which, except for those very limited circumstances outlined in

KSR, has consistently been held not to be the standard for obviousness under 35 USC § 103. Contrary to Applicants' argument, "obvious to try" can be used to support a conclusion of obviousness when chosen from a finite number of identified, predictable solutions, with a reasonable expectation of success. See MPEP § 2141 [R-6].

Applicants further submitted a Declaration under 37 C.F.R. § 1.132 to indicate that the K_d value obtained for heptyl-α-mannose is statistically significant. The Declaration further asserts that one of ordinary skill in the art would find a two order of magnitude decrease in the K_d of α-mannose with a n-pentyl group relative to unmodified mannose with an n-methyl or n-ethyl group to be unexpected. The Declaration has been carefully reviewed and is not persuasive in view of the new ground of rejection above. Contrary to the Declaration asserting that lengthening of the alkyl chain produces unexpected results, Silverman specifically teaches that lengthening of a saturated carbon side chain from one carbon to five to nine carbon atoms produces an increase in pharmacological effects. Thus, the Declaration of Dr. Julie Bouckaert is ineffective to rebut the *prima facie* case herein.

Conclusion

No claim is allowed. This rejection is made NON-FINAL due to the new/modified grounds of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-

270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

/SCARLETT GOON/
Examiner
Art Unit 1623